The risk of malignancy among biologic-naïve pediatric psoriasis patients: A retrospective cohort study in a US claims database

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Background: Little published literature exists regarding malignancy risk in pediatric psoriasis patients.

Objective: To compare malignancy risk in biologic-naïve pediatric psoriasis patients with a matched pediatric population without psoriasis.

Methods: This retrospective cohort study used IMS LifeLink Health Plan Claims data covering 1998-2008. Cancer incidence was compared with the US Surveillance, Epidemiology, and End Results (SEER) data using standardized incidence ratios (SIR), and between cohorts using Cox models.

Results: Among 9045 pediatric psoriasis patients and 77,206 comparators, 18 probable or highly probable cancers were identified. Pediatric psoriasis patients had a nonsignificantly lower incidence than comparators (hazard ratio [HR] 0.43, 95% confidence interval [CI] 0.05-3.54). The HR increased to 1.67 (95% CI 0.54-5.18) when cancer diagnosed during the first 90 days of follow-up was included. The pediatric psoriasis cohort had a significantly increased lymphoma rate compared with SEER (SIR 5.42, 95% CI 1.62-12.94), but no significant increase relative to the comparator cohort.

Limitations: Misclassification of disease and outcome might have occurred with patients in the claims database.

Conclusion: Patients with pediatric psoriasis showed no significant increase in overall cancer risk compared with those without psoriasis. A potential increased risk for lymphoma was observed when compared with the general population. (J Am Acad Dermatol 2017;77:293-301.)

Key words: cancer; cohort study; epidemiology; incidence rates; lymphoma; pediatric psoriasis.

The annual incidence of pediatric psoriasis has been estimated at 33.2/100,000 persons.[1] Prevalence estimates range from 0.19% to 0.71%[2,3] and increase with age, even among pediatric populations.[2-4]

In the past decade, biologics such as tumor necrosis factor (TNF) inhibitors were approved for treatment of adult psoriasis in the United States.[5-7] To date, some biologics are approved for pediatric psoriasis in Europe but not in the United States.[8] TNF inhibitors are approved to treat other pediatric diseases such as juvenile idiopathic arthritis and Crohn disease.[9,10] Concerns about the safety of TNF inhibitors, including the potential increased risk for lymphoma and other cancers for children and adolescents, has been the focus of regulatory reports.[11,12]

Adults with psoriasis have an increased risk for lymphoma and, less consistently, other cancer types.[13] Gelfand et al found that psoriasis patients

From Pfizer Inc, Collegeville[a]; and Evidera, Waltham.[b]
Funding sources: Supported by Pfizer Inc.
Conflicts of interest: Dr Gu is employed by Pfizer and owns stock and stock options in Pfizer. Dr Nordstrom is employed by Evidera, which received funding from Pfizer for the study and the development of the manuscript.
Accepted for publication March 29, 2017.

Reprints not available from the authors.
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Published online June 13, 2017.
0190-9622/$36.00

http://dx.doi.org/10.1016/j.jaad.2017.03.044

are at increased risk for lymphoma (relative risk 2.95, 95% confidence interval [CI] 1.83-4.76) compared with those without psoriasis.[14] The epidemiology of cancer in pediatric psoriasis patients is unknown. Given concerns regarding malignancy risks with TNF inhibitors, it is important to examine cancer risks in the pediatric psoriasis population not treated with biologics to establish a baseline for evaluating the risk associated with biologics. This retrospective cohort study investigated the incidence of cancer in a large, claims-based pediatric psoriasis population and a matched pediatric population without psoriasis.

CAPSULE SUMMARY

- Adult psoriasis is associated with increased risk for lymphoma and other cancers.
- This retrospective cohort study found some evidence of an increased lymphoma risk with pediatric psoriasis when compared with the general population.
- Further investigation is warranted in different, large pediatric populations with a longer duration of follow-up.

METHODS

Cohort definition

Data were obtained from the IMS LifeLink Health Plan Claims Database, a largely commercially populated database including longitudinal inpatient and outpatient medical and pharmaceutical claims data and enrollment information.

The pediatric psoriasis cohort included incident and prevalent psoriasis cases occurring from January 1, 1998, through November 2, 2007. Data were extracted through January 31, 2008, allowing a minimum of 91 days' follow-up for the latest patients.

Pediatric psoriasis patients had at least 2 evaluation and management (EM) claims with International Classification of Diseases, Ninth Revision (ICD-9) code 696.xx, an initial diagnosis at age <18 years, and a claim for psoriasis-specific drugs or procedures, including topical therapy (coal tar, salicylic acid, calcitriol, calcipotriene, calcipotriene plus betamethasone dipropionate, tazarotene, anthralin, corticosteroids, tacrolimus), light therapy (ultraviolet light therapy, other phototherapy, therapeutic photopheresis, laser phototherapy, phototherapy services), or systemic nonbiologic therapy (methotrexate, retinoids [acitretin, isotretinoin], cyclosporine).

The comparators had no EM claims for psoriasis. Each pediatric psoriasis patient was matched with up to 10 comparators on age, sex, region, duration of enrollment (within 6 months), and eligibility (ie, membership in the health plan) on the same date as the matching pediatric psoriasis patient's cohort entry date.

The cohort entry date for a pediatric psoriasis patient was the latest of the dates for the first claim for psoriasis treatment, second psoriasis EM claim, calendar date January 1, 1998, or enrollment into the database plus 90 days. The cohort entry date for comparator was the same as the corresponding matched pediatric psoriasis patient.

To increase the probability that any cancer events during follow-up were truly incident cancers, at least 90 days of continuous observation time both before and after cohort entry were required. The first 90 days after cohort entry were not included in the eligible outcome period.

Patients meeting the following criteria before cohort entry were excluded: treated with biologic medication (including etanercept, infliximab, adalimumab, anakinra, abatacept, alefacept, rituximab, or certolizumab); had a diagnosis of cancer or genetic syndromes that increase cancer risk (including familial polyposis syndrome, albinism, ataxic telangiectasia, Fanconi syndrome, Bloom syndrome, Down syndrome), or comorbidities that predispose one to cancer (including organ transplantation or HIV) (Supplemental Table I; available at http://www.jaad.org).

Outcomes

Patients were followed for outcomes beginning 91 days after cohort entry until the earliest of initiation of biologic treatment, first occurrence of a comorbidity that predisposes one to cancer (ie, organ transplantation or HIV), disenrollment from the health plan, or end of study (January 31, 2008). Enrollment gaps of a maximum of 1 month were permitted during follow-up.

The primary outcome was a diagnosis of any malignancy, excluding nonmelanoma skin cancer (NMSC) and carcinoma in situ. The secondary outcome was all invasive malignancies including NMSC. For each patient with an EM or inpatient hospital claim with an ICD-9 code indicating any malignant neoplasm during follow-up, we produced a claims profile listing all diagnoses, procedures, and drugs in chronologic order. Two clinicians blinded to the cohort (pediatric psoriasis diagnosis and treatments) reviewed the patient profiles to determine which cases were possible, probable/highly probable, or not cancer events. NMSC and cancers occurring during the first 90 days after cohort entry